

LISTING OF THE CLAIMS

A detailed listing of all claims that are, or were, in the present application, irrespective of whether the claim(s) remains under examination in the application are presented below. The claims are presented in ascending order and each includes one status identifier.

1. (Previously Presented) A synthetic, soluble, endogenous complex comprising at least one component A and at least one component B, whereby component A comprises a binding domain for extra-cellular surface structures that internalize upon binding of component A of said complex, and component B has a constitutive catalytic kinase activity to affect cell biosynthesis and/or signaling, wherein the complex is synthetic, soluble, and endogenous.

2. (Previously Presented) The complex according to claim 1, whereby the component A is selected from the group of actively binding structures consisting of antibodies, antibody derivatives, antibody fragments synthetic peptides, scFv, mimotopes, carbohydrates, lipids, nucleic acids, peptides, vitamins, small molecules with up to 100 atoms with receptor-binding activity, peptidic molecules, non-peptidic molecules, cell surface carbohydrate binding proteins lectins, calnexins, c-type lectins, l-type lectins, m-type lectins, p-type lectins, r-type lectins, galectins natural ligands to the cluster of differentiation (CD) antigens, CD30, CD40, cytokines, chemokines, colony stimulating factors, type-1 cytokines, type-2 cytokines, interferons, interleukins, lymphokines, monokines, adhesion molecules, and their derivatives or mutants.

3. (Previously Presented) The complex according to claim 1 wherein component A is selected from the group of passively binding structures consisting of allergens, peptidic allergens, recombinant allergens, allergen-idiotypical antibodies, autoimmune-provoking structures, tissue-rejection-inducing structures, immunoglobulin constant regions and derivatives, mutants or combinations thereof.

4. (Previously Presented) The complex according to claim 1 wherein the component A is bound to the extra-cellular surface structure.

5. (Previously Presented) The complex according to claim 1, wherein component A comprises two or more of the binding domains.

6. (Previously Presented) The complex according to claim 1, wherein the component B constitutive catalytic kinase activity comprises at least one member of the group consisting of eukaryotic protein kinase (ePK) superfamily, histidine protein kinase (HPK) superfamily and atypical protein kinase (aPK) superfamily.

7. (Previously Presented) The complex according to claim 1, wherein the component B constitutive catalytic kinase activity comprises eukaryotic protein kinase comprising
(i) a calcium/calmodulin-regulated (CaM) death-promoting kinase that is selected from the group consisting of death-associated protein kinase (DAP-kinase, DAPk), DAP kinase-related protein kinase 1 (DRP-1), also named DAP-kinase 2 (DAPk2), DAP like kinase/Zipper

interacting protein kinase (Dlk/ZIP-kinase), and DAP kinase related apoptosis-inducing kinase (DRAK1 and DRAK2) families,

(ii) a calcium/calmodulin-regulated (CaM) death-promoting kinases-like (CAMKL) family member that is selected from the group consisting of protein kinase AMP-activated alpha 1 catalytic subunit (PRKAA1), protein kinase AMP-activated alpha 2 catalytic subunit (PRKAA2), BRSK1 and BRSK2, CHK1 checkpoint homologue (CHEK1), hormonally upregulated Neu-associated kinase (HUNK), serine/threonine kinase 11 (Peutz-Jeghers syndrome) (STK11), MAP/microtubule affinity-regulating kinase (MARK) 1-4, MARKps 01-30, likely ortholog of maternal embryonic leucine zipper kinase (KIAA0175), PAS domain containing serine/threonine kinase (PASK), NIM1, QIK and SNRK,

(iii) a death-domain receptor interacting protein kinase (RIP-kinase) family member that is selected from the group consisting of RIP-kinase 1, RIP-kinase 2, RIP-kinase 3 and RIP-kinase 4, ankyrin repeat domain 3 (ANKRD3) and SqK288,

(iv) a multifunctional CaM kinase family member that is selected from the group consisting of CaM kinase I, CaM kinase II, microtubule affinity-regulating kinases (MARK), microtubule affinity-regulating kinases-like 1 (MARKL1), CaM kinase IV, and CaM kinase subfamilies,

(v) a dedicated CaM kinase selected from the group consisting of Myosin light chain kinase (MLC_k), phosphorylase kinase and CaM kinase III,

(vi) a mitogen-activated protein kinase (MAPK) family member selected from the group consisting of extracellular signal-regulated kinases (ERK), c-JUN NH₂-terminal protein kinases (JNK), nemo-like kinase (NLK) and p38 kinase subfamilies,

(vii) a cyclin-dependent kinase (CDK) family member selected from the group consisting of cell cycle related kinase (CCRK), cell division cycle 2 (CDC2), cyclin-dependent kinases (CDK) 1-11, PCTAIRE protein kinase (PCTK) 1-3, PFTAIRE protein kinase (PFTK) 1-2 and cell division cycle 2-like 1 (PITSLRE proteins),

(viii) a eukaryotic translation initiation factor 2-alpha kinase 3 (EIF2AK3) family member selected from the group consisting of protein kinase interferon-inducible double stranded RNA (dsRNA) dependent (PKR) subfamily, or

(ix) derivatives, mutants or combinations thereof.

8. (Previously Presented) The complex according to claim 1, wherein the component B constitutive catalytic kinase activity comprises histidine protein kinase selected from a HPK 1-11 family.

9. (Previously Presented) The complex according to claim 1, wherein the atypical protein kinase (aPK) superfamily comprises

(i) an alpha protein kinase family member selected from the group consisting of eukaryotic elongation factor-2 kinase (eEF-2k), myosin heavy chain kinase (MHC-kinase), eukaryotic translation initiation factor 2 alpha kinase 1 (E2K1) and channel kinase (Chak1 and Chak2) subfamilies,

(ii) a Fas-activated s/t kinase (FASTK) family member selected from the group consisting of FASTK subfamily,

- (iii) a protein tyrosine kinase 9 (A6) family member selected from the group consisting of A6 and protein tyrosine kinase 9-like (A6r) subfamilies,
- (iv) a p21-activated protein kinases (PAK) family member consisting of alpha-PAK (PAK1), beta-PAK (PAK3) and gamma-PAK (PAK2, PAK1),
- (v) an Interleukin-1 (IL-1)-receptor-associated kinase (IRAK) family member selected from the group consisting of IRAK-1, IRAK-2, IRAK-3 and IRAK-4 subfamilies, or
- (vi) derivatives, mutants or combinations thereof.

10. (Previously Presented) The complex according to claim 1, whereby the constitutive kinase activity of component B directly activates or inactivates components of a cell-regulatory pathway through phosphorylation, acetylation, methylation, prenylation, or sulfation, thereby altering the function, gene expression, or viability of a target cell that binds component A.

11. (Previously Presented) The complex according to claim 1, wherein component B comprises DAP-kinase 2 (DAPk2) or a derivative thereof.

12. (Previously Presented) The complex according to claim 1, wherein component B comprises eukaryotic elongation factor-2 kinase (eEF-2k) or a derivative thereof.

13. (Previously Presented) The complex according to claim 1, comprising one or more supplementary component S which regulates protein biosynthesis on the transcription and/or translation level, and/or enables purification and/or detection of the complex,

and/or facilitates translocation of at least component B into the target cell, and/or intracellular separation and/or activation of component B,

wherein the component S is selected from the group of inducible promoters, leader sequences, affinity tags, His tags, translocation domain, amphiphatic sequences and synthetic pro-granzyme B.

14. (Previously Presented) The complex according to claim 1, wherein the components A and B are chemically coupled and/or genetically fused to each other.

15. (Previously Presented) The complex according to claim 1 comprising amino acid sequence SEQ ID NO: 2, SEQ ID NO: 4 or SEQ ID NO: 6.

16. (Previously Presented) A nucleic acid molecule coding for the complex of claim 15.

17. (Previously Presented) A composition comprising a cell or non-human organism transformed or transfected with the nucleic acid molecule according to claim 16.

18. (Previously Presented) The composition of claim 17, wherein the organism or the cell is a prokaryote, a lower eukaryote a higher non-human eukaryote, or a primary or cultivated mammalian cell.

19. (Previously Presented) A method for influencing the growth and/or the physiology of cells comprising culturing the cell of claim 17 under conditions supporting the activity of the complex.

20. (Cancelled).

21. (Previously Presented) A medicament comprising the complex of claim 1 disposed in a physiologically acceptable dosage form.

22-24. (Cancelled)

25. (Previously Presented) The complex of claim 1 wherein the constitutive catalytic kinase causes cell death after internalization of the complex into the cell.

26. (Previously Presented) The complex of claim 2 wherein the component A binds to a cluster of differentiation (CD) antigen, cytokine receptor, hormone receptor, growth factor receptor, ion pump, or channel-forming protein.

27-28. (Cancelled)

29. (Previously Presented) The complex of claim 1 wherein components A and B are peptides.

30. (Cancelled)